had a stillbirth rate of 10.1 per 1000. A decline in the hospital stillbirth rate for this minimal-risk group from 11.7 to 10.1 per 1000 is relatively less than that achieved outside, from 4.2 to 3.4—hardly an impressive vindication of the current policy of moving towards hospitalisation for all.

Thus the more recent evidence on stillbirths fails to support the conclusion drawn by Mrs Fedrick and Professor Butler from 1958 data. The need for further research is as great as ever.

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¹ Tew, M. *New Society*, 1977, **39**, 120.

² Tew, M., *Journal of the Royal College of General Practitioners*, 1977, **27**, 689.

³ Tew, M., in *The Place of Birth*, ed S Kitzinger and J Davis. London, Oxford University Press, 1978.

⁴ Office of Population Censuses and Surveys, *Registrar General's Statistical Review of England and Wales for 1969*. London, HMSO, 1971.

⁵ Registrar General, unpublished return for 1975.

Hospital laboratory computing

SIR,—Your leading article (18 February, p 387) and Professor I D P Wootton (1 April, p 851) are right in saying that medical computing systems that can easily be transferred to other sites are highly desirable. I would, however, like to question whether we yet have such systems for hospital laboratory computing in Britain. Dr M D Buckley-Sharp (4 March, p 577) lists a number of recipient laboratories of the excellent Phoenix system from the Hammersmith Hospital, but he does not say if any of them are actually being served by their computer system on a routine basis. As I have said before,¹ we should not accept that a system is a general one until it has proved itself in routine use at a number of recipient sites.

Simple transfer of medical computing systems has proved an elusive goal in the past, but it is still one which we should try to achieve. Success in overcoming the problems it presents should be carefully and accurately recorded for the benefit of others trying to achieve it. May we know, therefore, how many laboratories now routinely use Phoenix (or a derivative of it) and for how long they have done so?

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¹ Coles, E C, *Journal of the Royal College of Physicians of London*, 1974, **8**, 355.

Drug information services

SIR,—The total number of inquiries received by the regional drug information centres, as reported by Dr F N Leach (25 March, p 766), represents only a small percentage of the total number of inquiries made annually to drug information centres and, if taken alone, underestimates the advisory role of these services. The results of a small survey will illustrate this point.

The survey was conducted during a two-week period in 1976 and detailed all inquiries received across a teaching district of 1700 acute beds serving most specialties. There is an active ward pharmacy programme at each of the hospitals within the district and a department of clinical pharmacology and therapeutics at the hospital in which a specialist

pharmacy-based district drug information service has been developing over four years. The extrapolated district total of inquiries for 1976 was 5800 compared with a total of 8584 from the eight regional centres listed by Dr Leach. During the survey period the drug information pharmacist dealt with 13% of all inquiries, the rest being answered by pharmacists in the course of their work; 10% were made directly to the centre and 3% referred. However, within the hospital in which it is based the centre answers 33% of inquiries. During the survey period 8% of inquiries arose outside the district.

The types of inquiry made to the district drug information service were very similar to those quoted by Dr Leach. The highest proportion came from hospital pharmacists as a result of clinical problems met on the ward rounds. This demonstrates the interception of inquiries by district and area centres. Non-clinical staff accounted for nearly as many inquiries as clinicians. A multidisciplinary approach is required for the provision of a comprehensive drug information service, which includes clinical, pharmaceutical, and scientific problems.

The national usage of drug information resources and the contribution of local drug information pharmacists is greater than Dr Leach's paper, concentrating on the regional centres only, would suggest.

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British standard insulin syringe

SIR,—Let us stop, look, listen, and think—let us not be stampeded and corralled into accepting U-100 (100 U/ml) insulin as the only one, with all other strengths banned (Drs B F Brearley and J Mackie, 18 March, p 713). This would irrevocably condemn all insulin-dependent diabetics to one system of varying (expensive) syringes and all its drawbacks. One system, like a monopoly, could become a tyranny.

Let the positive aim of this country be the acceptance of U-100 as a new factor for assessment for improved insulin administration to patients and not be abused as a weapon to remove the possibility of better techniques. One technique I suggest is to combine the use of U-20 and U-100 using the present standard syringe only, with its 20 graduation marks. For U-100 one graduation mark would measure 5 U and for U-20 1 U of insulin, this information to be precisely engraved on the syringe.

Thus the largest part of one injection could be measured from U-100 in multiples of 5 U and the balance of less than 5 U from U-20, which would give accurate end-point measurement to 1 U per graduation for the dose. For several reasons precision measurement of dose is of great importance. Small doses would be measured from U-20 insulin up to 20 U. I have used this simple technique on myself for many years with U-80 and U-40. These would be withdrawn when U-100 and U-20 became available.

The advantages for the patient are the lower volume given by U-100 and great precision of measurement by U-20; the use of one syringe only for all doses of insulin, and therefore no added stress; and for the NHS and our country

no massive additional cost for multiple differing syringes and holders.

Adopting the American technique, banishing all insulin concentrations except U-100, excludes this suggested (British) technique. Adopting the suggested (British) technique of one standard insulin syringe and of two insulin concentrations, U-100 and U-20, does not prevent anyone adopting the American technique, but in the beginning they should have to buy the special syringes required.

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Outpatient chemotherapy for breast cancer

SIR,—We wish to comment on the letter from Dr R Bell and others (1 April, p 857) concerning the oral administration of 400-mg doses of methotrexate.

The statement that the patients' supreme effort of swallowing 10 tablets every hour for 16 h results in similar blood levels to those achieved by infusion of the drug is not supported by hitherto published evidence. Although doses of less than 30 mg/m² have been shown to be nearly completely absorbed from the gastrointestinal tract,^{1,2} absorption is protracted and incomplete with doses of 80 mg/m² or more, leading to plasma levels less than one-tenth of those achieved after intravenous administration.^{3,4} If this is, in fact, the case it is not surprising that in the study by Dr Bell and his colleagues toxicity was relatively mild. However, the cytotoxic efficacy of the drug may well be open to question.

In answer to the request for a higher-strength tablet, may we point out that we are in the process of developing a 10-mg tablet? In addition we can supply a formula from which a 2 mg/ml syrup preparation can be made. Preliminary pharmacological and stability data for this formulation have been published.⁴

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¹ Henderson, E S, *et al*, *Cancer Research*, 1965, **25**, 1018.

² Huffman, D M, *et al*, *Clinical Pharmacology and Therapeutics*, 1973, **14**, 572.

³ Wan, S H, *et al*, *Cancer Research*, 1974, **34**, 3487.

⁴ McVie, J G, *British Journal of Cancer*, 1977, **36**, 417.

Intra-articular steroids

SIR,—Your recent leading article on this subject (11 March, p 600) presented highly agreeable and balanced advice to clinicians, since many previous reports concerning this subject have been paradoxical at least to some extent. However, it seems to us that the excess use of intra-articular corticosteroid injections in sports medicine as "pain-killers," especially in knee injuries, should be criticised.

A recent experimental study on rabbits¹ suggested that intra-articular betametasone seemed to have a protective effect against early articular cartilage degeneration in the knee joint when the rabbits were subjected to strenuous exercise. However, the protective effect of both intra-articular and intramuscular glycosaminoglycan polysulphate injections

could be evaluated as even better. As the possibility for iatrogenic damage after intra-articular cortisone injections has been reported²⁻⁶ to be higher than was observed after intra-articular or especially intramuscular glycosaminoglycan polysulphate therapy it seems justified to suggest this treatment in cases of painful knee joints after sports trauma and strenuous exercise.

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- ¹ Santavirta, S., Arstila, A. U. and Sorvari, T., in preparation.
² Behrens, E., Shepherd, N., and Mitchell, N., *Journal of Bone and Joint Surgery*, 1975, **57A**, 70.
³ Mankin, H., and Genger, K., *Journal of Bone and Joint Surgery*, 1966, **48A**, 383.
⁴ Salter, R., Gross, A., and Hall, J., *Canadian Medical Association Journal*, 1967, **97**, 374.
⁵ Steinberg, C., et al., *Journal of the American Medical Association*, 1962, **181**, 851.
⁶ Stohr, A., and Hellinger, J., *Beiträge zur Orthopädie und Traumatologie*, 1977, **24**, 330.

Septic abortion and IUCDs

SIR,—We were interested in the comments of both Dr E. S. B. Wilson and Mr W. G. Mills (18 March, p. 719) on our report of septic abortion and septicaemia in a Gravigard (Copper-7) user (25 February, p. 481). In reply to Dr Wilson we agree that culture of a high vaginal swab (HVS) is unsatisfactory in diagnosing the bacteriological cause of pelvic inflammatory disease (PID) and indeed one of us has previously drawn attention to this point.¹ However, in our report we were referring to the intrauterine infection of products of conception and, while an intracervical or intrauterine sample may have been preferable, a HVS gives a picture of the bacterial flora of the upper vagina from which the infecting agent will have ascended into the uterus.

Dr Wilson has obtained pure cultures of bacteria from intrauterine contraceptive devices (IUCDs) removed from patients with signs and symptoms of pelvic infection. However, PID is difficult to diagnose without laparoscopy² and doubt must therefore exist as to whether these cultures necessarily represent bacteria causing tubal infection. Although contamination by vaginal organisms can be avoided by careful removal, it is impossible to avoid contaminating the IUCD with cervical mucus during its passage through the cervical canal and the cultures may merely represent the normal flora of the lower canal.

We cannot offer Mr Mills any further information on the time interval since insertion or on the length of the tail. However, although with other devices excessive length of tail is unlikely to be the explanation for its continued presence in the vagina at 16 weeks' gestation, the Gravigard is a special case. It differs from other current devices in that as supplied by the manufacturers the tail forms a loop alongside the device predisposing to several problems after insertion.³ If the Gravigard is fitted with the loop of tail left in the uterus, as is now recommended, the total length of tail is greater than that of other devices. As the uterus enlarges during pregnancy this slack may need to be taken up before the vaginal end

of the tail is pulled into the cavity. Once the tail has disappeared the bridge between the sterile uterus and the vagina with its organisms has been broken. Our reason for cutting the tail flush with the external os if the device cannot be removed is to reduce the time that it is in contact with the vagina.

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- ¹ Sparks, R. A., and Davies, A. J., *British Journal of Venereal Diseases*, 1976, **52**, 178.
² Jacobson, L., and Westrom, L., *American Journal of Obstetrics and Gynecology*, 1969, **105**, 1088.
³ Sparks, R. A., *British Medical Journal*, 1977, **2**, 1351.

Problems with IUCD tails

SIR,—Further to my letter (19 November, p. 1351) and that of Mr Geoffrey Chamberlain (28 January, p. 237), I should like to describe another problem with IUCD tails, which may be previously unreported.

A 32-year-old multiparous patient was seen for a routine IUCD check and the tail of the Lippes loop, which had been fitted six years previously, was protruding not from the external cervical os but from the vaginal surface of the upper lip of the cervix 7.5 mm from the os. The cervix was healthy with squamous epithelium up to the os—that is, there was no columnar epithelium outside the canal forming an "erosion." Presumably an erosion had previously been present and during the replacement of the columnar epithelium by squamous epithelium the metaplastic squamous epithelium had grown over the tail incorporating it into the cervix. The device was removed by pulling on the tail, which easily cut through the epithelium covering it. This complication is presumably less likely to occur with copper devices, which are routinely replaced every few years.

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Amniocentesis for the 35s and over

SIR,—There is currently uncertainty about the selection of pregnant women who should be offered amniocentesis. Galjaard¹ has stated that "some centres, as in Scandinavia, accept all women over 35, others take 40 as the limit and most groups, including our own, consider the age of 38 and older as an indication for amniocentesis."

The findings from 599 amniocentesis specimens received in the department of pathology from patients aged 35 years and over are shown in the table. These include 17 patients aged 35-39 and 11 patients aged 40 or more who had had a previous child with a chromosomal abnormality. There were also 23 patients aged 35-39 and five patients aged

40 or more who had a family history of neural tube defect. The prevalence of chromosomal abnormalities in mothers over 40 years was 6.15%. However, in mothers aged 35-39 there was a relatively high prevalence of abnormalities (1.98%), much higher than that cited, for instance, by Philip *et al.*² (0.2%), which has already been commented upon.³ We have diagnosed only one trisomy 21 where there has been a previously affected sibling.

Trisomy 21 was the most common abnormality in our series and it is of note that most of the cost-benefit analyses reviewed by Mikkelsen *et al.*⁴ were based on the prevalence of this syndrome. It has already been observed that there is a discrepancy between the prevalence of this syndrome as detected on amniocentesis and its estimated prevalence in a liveborn population.^{5,6} This may ultimately be explained following post-mortem chromosomal surveys of late abortions and stillbirths. Nevertheless, it would be unwise to allow this discrepancy to influence our judgment regarding the cost benefit of amniocentesis in women at different maternal ages. We consider that our results highlight the necessity for more widespread application of amniocentesis in the 35 and over age group. However, the ultimate decision should rest with the parents and the availability of clinical and laboratory expertise.

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- ¹ Galjaard, H., in *Towards the Prevention of Fetal Malformation*, ed J. B. Scrimgeour. Edinburgh, University Press, 1978.
² Philip, J., Bang, J., and Madsen, M., *British Medical Journal*, 1977, **2**, 1117.
³ Steven, J. D., and Scrimgeour, J. B., *British Medical Journal*, 1978, **1**, 301.
⁴ Mikkelsen, M., Nielsen, G., and Rasmussen, E., in *Towards the Prevention of Fetal Malformation*, ed J. B. Scrimgeour. Edinburgh, University Press, 1978.
⁵ Ferguson-Smith, M. A., *Lancet*, 1976, **2**, 252.
⁶ Bain, A. D., et al., *Lancet*, 1976, **2**, 375.

Why blame the pill?

SIR,—I note with concern that deaths from thrombosis occurring in young and middle-aged women who are on the contraceptive pill are being increasingly reported to the coroner and verdicts of accidental death are being returned. As there is no pathological feature to distinguish these cases from other cases of thrombosis not associated with this drug it would appear that these verdicts are based on the slight statistical increase in deaths from these causes noted in the various surveys of the contraceptive pill. I am surprised, therefore, not to have read of any deaths from bronchogenic carcinoma being the subject of an inquest in view of the fact that the link between

Chromosomal abnormalities in 599 amniocentesis specimens from patients aged 35 and over

Maternal age (years)	Total analysed 1975-7	Chromosome abnormality			Totals	Percentage abnormal
		Trisomy 21	Trisomy 18	Other*		
35-39	404	4	2	2	8	1.98
≥40	195	7	3	2	12	6.15
Totals	599	11	5	4	20	3.34

*These were: for age 35-39 : 47,XY,+mar; 47,XXX
for age ≥40 : 46,XX/47,XX,+r(mar); 45,X